In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 15-104V

(to be published)

JAMES AND BRANDY RILEY, on behalf of E.R., a minor,	*	Chief Special Master Corcoran
Petitioners,	*	Filed: August 31, 2021
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Mark Sadaka, Sadaka Associates LLC, Englewood, NJ, Petitioner.

Lara Englund, U.S. Dep't of Justice, Washington, DC, Respondent.

ENTITLEMENT DECISION[1]

On February 2, 2015, James and Brandy Riley filed a petition seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program")[2] alleging that their daughter, E.R., experienced the reactivation of varicella virus due to three vaccines administered to her on February 20, 2012—the varicella, measles-mumps-rubella ("MMR"), and diphtheria-

[1] This Decision will be posted on the Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means that the Decision will be available to anyone with access to the internet.** As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Decision will be available to the public in its current form. *Id*.

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

tetanus-acellular pertussis ("DTaP") vaccines. Petition (ECF No. 1) at 1.

The matter was previously assigned to a different special master, who determined that the claim could be efficiently resolved via ruling on the record, and both parties have filed briefs in support of their respective positions. *See* Petitioners' Brief, dated August 12, 2020 (ECF No. 91) ("Mot."); Respondent's Opposition, dated December 14, 2020 (ECF No. 93) ("Opp."); Petitioners' Reply, dated January 22, 2021 (ECF No. 95) ("Reply"). The case was thereafter reassigned to me. Order, dated January 26, 2021 (ECF No. 96).

After consideration of the briefs plus the medical records and expert reports, I deny entitlement in this case. The record best supports the conclusion that the blistering and lesions E.R. experienced post-vaccination reflected a herpes simplex virus ("HSV") infection—*not* reactivation of varicella, and hence not likely associated with or attributable to the varicella vaccine. Because the entirety of Petitioners' causal theory rests on a determination that E.R.'s rash and blistering constituted a "recurrent varicella-zoster infection at the lips" (Mot. at 10), the failure to prove this injury contention is fatal to the claim.

I. Factual Background

Pre-vaccination History and Events Around Time of Vaccination

E.R.'s pre-vaccination history largely does not bear on this matter—other than the fact that she received a combined vaccine (Proquad) containing the varicella and MMR vaccines at her one-year checkup on January 22, 2009. Ex. 1 at 1, 218. This appears to be the first time E.R. received either vaccine, and there is no evidence in the record before the date of the vaccinations at issue of any reactivation of varicella in the ensuing three-year period.

On February 20, 2012, E.R. (now four years old) saw her pediatrician for a routine check-up and received another Proquad dose, along with DTaP, influenza, and polio vaccines. Ex. 1 at 1. Eleven days later (March 2, 2012), E.R. saw her pediatrician for a red blister on her upper lip that was reported to have persisted for one and one half weeks (and thus likely first appeared February 21st or 22nd—a day or two after the vaccinations in question), plus another blister that was just starting to appear on her lower lip. *Id.* at 214-15. Mrs. Riley also reported episodes of vomiting and diarrhea two days prior to this visit. *Id.* The impression was an HSV infection, "likely fever blister." *Id.* Mrs. Riley was advised to return if E.R.'s symptoms worsened. *Id.*

In March and April 2012, E.R. was treated for an ear infection. Ex. 1 at 207-13. Outbreaks of the blistering at this time were controlled by Zovirax cream prescribed by E.R.'s pediatrician. Ex. 3 at 3. There are no other medical records for the remainder of 2012 filed in this case

documenting treatment efforts for these blisters by Petitioners.

Concerns for Persistent HSV Infection in 2013

Approximately one year later, on February 19, 2013, E.R. was seen by her pediatrician for treatment of a chronic HSV infection. Ex. 1 at 204-05. Mrs. Riley directly stated her concern that the persistent infection had been caused by the varicella vaccine administered almost a year before. *Id.* Examination showed several erosive lesions on the lips and several erythematous based honey-crusted lesions around the nose and chin. *Id.* The treater impression was nevertheless HSV, and it was deemed necessary to "rule out" immunodeficiency disorders. *Id.* E.R. was prescribed acyclovir.[3] *Id.* E.R. was seen for a follow-up visit approximately a week later, on February 28, 2013. *Id.* at 198-99. The acyclovir treatment had initially resolved her outbreak, but within 24 hours of the last dose three new lesions had appeared. *Id.* E.R. was also experiencing white patches in her mouth and inner lips that were diagnosed as oral thrush. *Id.*

A few weeks later, E.R. was taken to Cincinnati Children's Hospital Medical Center for an immunology evaluation with Patricia Fulkerson, M.D., on April 3, 2013. Ex. 2 at 152-54. On exam, Dr. Fulkerson noted rough red patches on E.R.'s lip at vermillion border under the right nostril, and small red patches scattered on her chin and mouth in sites where she previously had ulcers. *Id.* The diagnosis was recurrent cutaneous ulcers around E.R.'s mouth and chin for six weeks. *Id.* Blood testing revealed decreased "Natural Killer ("NK") cell function and positive varicella-zoster virus ("VZV") antibodies, but HSV antibodies, reflective of a current or resolved infection, were not detected. *Id.* at 178, 181, 188-89, 193. A mouth swab was also negative for HSV by polymerase chain reaction test ("PCR"). *Id.* at 191.

E.R. returned to Dr. Fulkerson for a follow-up visit on May 1, 2013. Ex. 2 at 221-25. Mrs. Riley again reported that the lesions had first appeared in February 2012, and persisted despite twelve months of topical acyclovir, worsening over a year's time. *Id.* An immune evaluation showed poor NK cell levels and T cell functional responses. *Id.* Labs were ordered to confirm reduced NK function. *Id.* Repeat testing for HSV antibodies again yielded negative results. Ex. 1 at 71. Later that same month, on May 24, 2013, E.R. was seen by her pediatrician for a swab of a new lesion. *Id.* at 71-76. The samples were inadequate to test for VZV or HSV by PCR, but viral cultures were negative for both viruses. *Id.*[4]

[3] Acyclovir is a synthetic acyclic purine nucleoside with selective antiviral activity; it is active against most known species of human herpesviruses, particularly against types 1 and 2, which cause herpes simplex. *Dorland's Illustrated Medical Dictionary,* 24 (33rd. ed. 2020) (hereinafter, "*Dorland's"*). It is used in the treatment of genital and mucocutaneous herpesvirus infections, and administered orally or topically. *Id.*

[4] Dr. Fulkerson had, however, noted in a prior medical record on May 1, 2013, that E.R.'s immune evaluation revealed a protective specific IgG level for VZV. Ex. 2 at 251.

On June 5, 2013, E.R. returned to Dr. Fulkerson, who opined in the relevant record from this visit that E.R.'s infection was "unlikely to be vaccine-derived varicella, but we do not have evidence that it isn't." Ex. 2 at 264-65. Lab tests confirmed prior evidence of a defect in E.R.'s NK cell function, however, although the etiology for it was unknown. *Id.* Petitioners were advised to continue treating E.R. with acyclovir. *Id.* Dr. Fulkerson saw E.R. again on July 17, 2013, and at this time Dr. Fulkerson expressed surprise that E.R. had been negative for evidence of a past HSV infection, given that she had active lesions consistent with HSV. *Id* at 320. E.R. had otherwise been doing well since her last visit and was advised to continue with acyclovir. *Id.*

Subsequent Treatment and Speculation Regarding Cause of HSV Infection

On September 12, 2013, E.R. saw Maria Lopez-Marti, M.D., a pediatric infectious disease specialist at Marshall Health in Huntington, West Virginia, for "recurrent HSV and immunodeficiency." Ex. 1 at 36-41. Dr. Lopez-Marti's impression was that E.R. "most likely has HSV infection that is localized to perioral region… It does not look like VZV that has a dermatomal distribution, but this pattern is not present here." *Id.* To confirm her suppositions, Dr. Lopez-Marti ordered a viral culture and PCR when E.R. had a new lesion. *Id.* Dr. Lopez-Marti noted that E.R. also had other cutaneous viral illnesses—viral warts and molluscum contagiosum, and one of the molluscum lesions was infected. *Id.* She recommended a switch from acyclovir to valacyclovir, which had better bioavailability and required less frequent does. *Id.* E.R. was also tested for HIV, which was negative. *Id*. at 36.

E.R. returned to Dr. Lopez-Marti two weeks later, on September 26, 2013. Ex. 1 at 30-34. She now had two new lesions, and they were tested by PCR—but results were negative for both HSV and VZV. *Id.* at 27, 29. E.R.'s parents reported that the doctors at Cincinnati Children's Hospital did not agree with the recommendation to switch to valacyclovir, so E.R. had not started that medication, but Dr. Lopez-Marti reiterated her treatment recommendation. *Id.*

On November 19, 2013, E.R. saw her pediatrician for sores on her tongue. Ex. 1 at 24-25. The assessment was oral thrush. *Id.* E.R. was referred to the rheumatology department for an evaluation of a possible autoimmune etiology of her oral lesions. Ex. 2 at 351-52. Testing for HSV IgG was again negative, although HSV IgM (which would be evidence of a more recent infection)[5]

[5] Immunoglobulin G, or "IgG," is the most common antibody, and it protects against bacterial and viral infections. Nemours KidsHealth, *Blood Test: Immunoglobulins (IgA, IgG, IgM)*, available at https://kidshealth.org/en/parents/test-immunoglobulins.html (last visited Aug. 12, 2021). IgG can take time to form after an infection or immunization. *Id.* Immunoglobulin M, or "IgM", first appears on the surface of B cells, and is the first antibody the body makes when it fights a new infection. *Id; Dorland's* at 908-09. IgM can activate the classic complement pathway and act as opsonins, triggering phagocytosis of the bound antigens by macrophages and

was in the indeterminate range. *Id.* at 115.

On January 15, 2014, E.R. was seen by Michael Henrickson, M.D., M.P.H., at Cincinnati Children's Hospital's Rheumatology Department. Ex. 2 at 77-83. E.R.'s tongue lesions were evaluated at this time, and the record notes the lesions were about 1 cm, raised and white, and uncomfortable, but not painful. *Id.* The assessment was cell-mediated immunodeficiency with recurrent HSV type 1 infections, biomechanical disorders (including generalized hypermobility and flexible pes planus) and recurrent minor aphthous ulcers, and obesity. *Id.* A telephone note from Dr. Fulkerson on January 27, 2014, stated that "despite her negative antibody titers, her response to acyclovir still suggests latent HSV infection." Ex. 35 at 19.

Records pertaining to treatment received after January 2014 make no further mention of the HSV blisters, and E.R. no longer appears to be taking any antiviral medications for their treatment. *See generally* Ex. 32-34. Petitioners' written witness submissions indicate that E.R. is currently doing much better, although when she does get sick or experiences stress, she will start to break out in sores in and around her mouth. *See* Mot. at 6.

II. Expert Opinions

A. *Dr. Vera Byers*

Dr. Byers provided three expert reports in support of Petitioners' claim. Report, filed Jan. 20, 2017 (ECF No. 41-1) ("Byers First Rep."); Report, filed Mar. 26, 2018 (ECF No. 58) ("Byers Second Rep."); Report, filed Jan. 28, 2020 (ECF No. 83) ("Byers Third Rep."). Dr. Byers opines that E.R.'s chronic, virally-induced dermatologic disorder was caused by or substantially contributed to by the vaccinations she received on February 20, 2012.

Dr. Byers received her bachelor's degree, master's degree in microbiology, and Ph.D. in immunology from the University of California, Los Angeles. Ex. 44 at 5, filed July 15, 2021 (ECF No. 99-1) ("Byers CV"). Before entering medical school, she completed two post-doctoral fellowships: one in protein chemistry at Abbott Labs in Chicago, Illinois, and the second in clinical and tumor immunology at the University of California, San Francisco ("UCSF"). *Id.* She then attended medical school and completed a three-year residency at UCSF, thereafter, becoming a member of the faculty there. *Id.* at 1, 4. Today, Dr. Byers is a medical toxicologist and consulting medical director at Immunology, Inc. of Incline Village, Nevada, and she has frequently served as

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neurtrophils. *Dorland's* at 908-09. Thus, the presence of IgM is deemed evidence of an active or current infection, while evidence of IgG suggests that a person already has some level of immunity derived from a resolved infection. *Knorr v. Sec'y of Health & Hum. Servs.*, No. 15-1169V, 2018 WL 6991548, at *4 n.7 (Fed. Cl. Spec. Mstr. Dec. 7, 2018).

an expert witness in lawsuits over the past fifteen years, including Vaccine Program cases. Byers CV at 2. She has also maintained several positions as an allergist and immunologist performing research and clinical trials in a variety of different areas. Byers CV at 2–4. Dr. Byers does not, however, have demonstrated specific research expertise in the study of varicella reactivation or HSV infections.

First Report

Dr. Byers began her first report with a summary of E.R.'s vaccination record and key laboratory tests. Byers First Rep. at 1. She then discussed E.R.'s pre-vaccination infectious disease history, which she characterized as "normal and benign." *Id.* at 2. But Dr. Byers concluded that E.R. "has a cell mediated deficiency resulting in recurrent episodes of blisters on and around the mouth, and of thrush on the tongue and inside cheeks which are large enough to interfere with speech because of their size." *Id.* at 3. In particular, she described E.R. as a "young girl [who] has a genetic immunodeficiency disorder affecting both the cytotoxic T cells and the NK cells." *Id.* Dr. Byers has not opined that this immunodeficiency was *itself* caused by the relevant vaccinations at issue in this case.

Dr. Byers proposed that the vaccines E.R. received in February 2012 were likely responsible for E.R.'s subsequent chronic HSV infection, presenting with the orolabial blisters substantiated in the medical record. E.R. was relatively well until she was four years old, despite apparently suffering from the above-referenced immunodeficiency. Byers First Rep. at 3. But the negative impact of this preexisting condition was likely thereafter triggered, since NK cell deficiencies usually manifest clinically when the patient becomes infected with a virus. *Id.*; J. Orange, *Natural Killer Cell Deficiency*, 132(3) J. Allergy Clin. Immunol. 515-526 (2013), filed as Ex. 14 on Jan. 23, 2017 (ECF No. 42-10). The VZV vaccine strain is generally well tolerated, but in rare cases has caused a severe disseminated life-threatening infection when given to people with immunodeficiency disorders, including patients with defective NK T cells. Byers First Rep. at 3; J. White, *Varicella-Zoster Virus Vaccine*, 24 Clin. Infectious Disease 753-63 (1997), filed as Ex. 5 on Jan. 23, 2017 (ECF No. 42-1).

Dr. Byers deemed it somewhat "scientifically unsound speculation to try to isolate a single component of the 9 separate vaccinations [E.R.] received on February 20, 2012 as the cause of her present illness." Byers First Rep. at 4. This was especially so given the fact that E.R. had already received numerous vaccines in the past, which Dr. Byers maintained "undoubtedly primed her defective immune system before the vaccinations that caused the clinical presentation of her immune deficiency disorder." *Id.* Nevertheless, she felt both the MMR and varicella components of the Proquad vaccine likely played a role, albeit for different reasons.

The MMR vaccine, she argued, would have an immunosuppressive impact, making an

aberrant immune response more likely. Byers First Rep. at 3. The varicella component, by contrast, was known to be associated with eczematous disease ("90 cases in a VAERS inquiry 01/16/2017"). *Id.* at 4. Dr. Byers also felt it significant that E.R. had received two doses of varicella vaccine (albeit three years apart)—allowing for the possibility that the vaccine-induced varicella strain introduced to E.R.'s system in 2009 could have remained latent in the nerves, reactivated thereafter by the immune response to the second dose. *Id.*

Finally, Dr. Byers attempted to rebut the conclusion that E.R. might simply be suffering from an HSV infection having nothing to do with vaccination. She noted that even if treaters had diagnosed an HSV infection (and the record in fact establishes they did), E.R. had tested negative for herpes simplex antibodies, and PCR testing of the lesions also produced negative results. Byers First Rep. at 3. Dr. Byers acknowledged that because E.R.'s lesions began after vaccination, it was possible that she had subclinical HSV which was reactivated by the immunosuppressive activity of the measles vaccines, but she deemed this unlikely because of the lack of any proven prior HSV infection. *Id.* She also cautioned that clinical tests for infectious diseases in a child with immunodeficiency must be carefully interpreted, since many routine tests depend on antibody formation. *Id.* Dr. Byers maintained however, that since E.R.'s immunoglobulin levels were normal, and because she demonstrated positive antibody response to varicella zoster, it was likely E.R. would have possessed HSV antibodies had she in fact suffered from such an infection. *Id.* Ultimately, Dr. Byers proposed that E.R.'s blisters were not caused by HSV, but instead represented vaccine strain VZV infection. *Id.*

Second Report

Dr. Byers's second report responded to the opinions offered by Respondent's expert, Dr. Hayley Gans. Dr. Byers questioned Dr. Gans's opinion that E.R.'s perioral lesions/blisters were most consistent with HSV from a clinical standpoint. Byers Second Rep. at 2. Dr. Byers countered that Dr. Gans had ignored the fact that E.R. never displayed antibodies to HSV, and that treaters were unable to obtain confirmatory evidence of HSV by either PCR or immunoglobulin production. *Id.* Dr. Byers simply deemed the absence of serologic proof of the infection to be damning to this conclusion, regardless of how the blisters appeared to treaters from a clinical standpoint.

In so arguing, Dr. Byers discounted the medical and scientific literature cited by Dr. Gans for the proposition that antibody testing for HSV could not be considered completely accurate in determining whether a person actually was so infected, offering a different item of literature in response. Byers Second Rep. at 3, *citing* R. Ashley, *Sorting Out the New HSV Type Specific Antibody Tests*, 77(4) Sex. Transm. Infect. 232-37 (August 2001), filed as Ex. A, Tab 12 on June 13, 2017 (ECF No. 51-2) ("Ashley"). Ashley noted that the performance characteristics of gold standard tests for the presence of HSV have yet to be established for children, and that no test for

antibodies to HSV-1 or HSV-2 can ever be considered completely accurate in determining whether a person has or has not been infected with HSV. *Id.* at 235. Dr. Byers added that Ashley was published in 2001, and HSV testing procedures had, in her opinion, advanced considerably since then. Second Byers Rep. at 3.

Next, Dr. Byers attempted to explain how the blisters E.R. had experienced could be consistent with a VZV/varicella reactivation infection despite how they were actually viewed by E.R.'s treaters. Byers Second Rep. at 4. As she noted, HSV and VZV are both Herpes-type viruses, and infections of them can cause disease in immunodeficient patients. They also, she maintained, can equally produce dermal and perioral lesions. *Id.* In addition, both viral illnesses respond to acyclovir, and after initial presentation both remain in dormant states within nerve cells. *Id.* As such, subsequent reactivation can result in similar presentations. *Id.* And the varicella vaccine package insert recognized the dangers posed by vaccination of an immunocompromised person like E.R. *Id.* at 3-4.

By contrast, E.R. had tested *positive* for VZV antibodies, indicating to Dr. Byers that E.R. was populated with latent vaccine strain virus in ganglionic neurons, having previously mounted an immune response. Byers Second Rep. at 3; S. Hambleton et al., *Risk of Herpes Zoster in Adults Immunized with Varicella Vaccine*, 197 J. of Infectious Disease S196-99 (2008), filed as Ex. 22 on Apr. 11, 2018 (ECF No. 59-6). Although the lesions themselves tested negative for VZV, as established both by culture testing and by PCR, Dr. Byers attributed that to the fact that the vaccine strain of the virus had likely been mutated by design, to reduce the possibility of replication. Second Byers Rep. at 3.

Dr. Byers also discussed the relevance of E.R.'s normal reaction to a prior MMR vaccination, and whether this was inconsistent with her assertion that the MMR component of the Proquad vaccine in February 2012 had contributed to her reaction due to its immunosuppressive nature. Byers Second Rep. at 4. She cited a case report involving a child who purportedly had a normal reaction to an initial MMR dose, but then developed varicella lesions upon either exposure to the wild type varicella or from re-vaccination. *Id.*; B. Uebe et al., *Herpes Zoster by Reactivated Vaccine Varicella Zoster Virus in a Healthy Child*, 161 Eur. J. Pediatr. 442-44 (2002), filed as Ex. 30 on Apr. 11, 2018 (ECF No. 60-4) ("Uebe"). Uebe, however, does not facially support this contention. The case discussed in Uebe is that of a healthy two year-old girl who developed herpes zoster infection, localized in three cervical dermatoma, after reactivation of VZV vaccine received 16 months before, and that had become latent in sensory ganglia. Uebe at 442-43. But Uebe does not comment on the role the prior administration of the MMR vaccine might have played in causing reactivation – and in fact makes no mention of the child's prior vaccination history (other than her receipt of a varicella vaccine).

Third Report

Dr. Byers's third report sought to answer questions posed by the special master formerly handling the case. She again described E.R. as immunodeficient, lacking a subpopulation of lymphocytes (NK cells) needed to eliminate exogenous pathogens, especially viruses. Byers Third Rep. at 1. In this context, two days after receipt of the MMR and varicella vaccines, E.R. developed lip blisters. *Id.* The resultant inflammation attributable generally to the impact of vaccination, together with the immunosuppression secondary to the effect of the MMR vaccine, was enough to cause the vaccine varicella latent in E.R. to reactivate. *Id.*; T. Mogensen et al., *Molecular Pathways in Virus-induced Cytokine Production*, 131 Microbiology and Molecular Biology Rev. 131-150 (2001), filed as Ex. 40 on Jan. 28, 2020 (ECF No. 85-3) ("Mogensen"). Mogensen describes HSV (wild virus, not vaccine) as characterized by a rapid life cycle, spreading with destruction of infected cells, and capable of establishing latency in sensory neurons, such that it could later be subject to reactivation. *Id.* at 132.

Dr. Byers continued to highlight evidence suggesting that a varicella reactivation post-vaccination could be anticipated, and was consistent with E.R.'s experience. She again referenced the package insert, which stated that a varicella-like rash could appear between 5-26 days after initial immunization. Byers Third Rep. at 2. In her opinion, the rash would be expected to appear even earlier where, as here, the existing latent vaccine strain was stimulated into action by the immunosuppressive qualities of the MMR vaccine (which E.R. had also just received). *Id.*; Uebe.

Dr. Byers also argued that varicella virus reactivation could occur anywhere on the body, including the lips, which are enervated by the maxillary branch of the trigeminal ("TG") nerve in the head.[6] Byers Third Rep. at 2; M. Warman et al., *Varicella Zoster Virus Infection Involving the Maxillary Branch of the Trigeminal Nerve*, 146(2) Harefuah 89-91 (2007) (article originally in Hebrew), filed as Ex. 41 on Jan. 28, 2020 (ECF No. 85-4) ("Warman"). Warman reviews the case history of a single young patient infected with VZV complicated by secondary bacterial infection of the ipsilateral hemiface. Warman at 89. However, Petitioners only filed the abstract of this article, not a full copy, preventing consideration of the extent to which the article truly supports Petitioners' claim. Warman also expressly notes that cranial nerves are *less* commonly affected by herpes zoster than those of the thorax and abdomen. *Id.* Dr. Byers nevertheless did not find that the location of E.R.'s blisters/lesions on her face undercut the conclusion that they reflected a VZV infection.

Finally, Dr. Byers again attempted to bulwark her contention about the trustworthy and reliable nature of serologic testing for HSV. In support, she provided a declaration concerning a conversation she had with Dr. Vincent Ricchiuti of LabCorp discussing LabCorp's goals when

[6] Trigeminal pertains to the fifth cranial nerve (nervus trigeminus). *Dorland's* at 1936.

running these kinds of tests. Byers Third Rep. at 2. The declaration recounts Dr. Ricchiutti stating to Dr. Byers that VZV-oriented testing is aimed at determining if an acute/recent infection exists, and does not seek to ascertain if the *vaccine* VZV strain is present. Affidavit, filed Jan. 28, 2020 (ECF No. 84-1). Thus, neither of these tests purport to measure for "vaccine reactivation" specifically, by distinguishing between the kind of strain at issue. Byers Third Rep. at 2.

B. *Dr. Hayley Gans*

Dr. Gans provided three expert reports on Respondent's behalf. Report, filed as Ex. A on May 23, 2017 (ECF No. 49-1) ("Gans First Rep."); Report, filed as Ex. C on May 24, 2018 (ECF No. 62-1) ("Gans Second Rep."); Report, filed as Ex. D on Feb. 24, 2020 (ECF No. 86-1) ("Gans Third Rep."). Dr. Gans opined that E.R.'s NK cell deficiency, and not the varicella vaccine or the immunosuppressive impact of any other vaccine, predisposed her to recurrent HSV orolabial lesions. Gans First Rep. at 11; Gans Second Rep. at 1.

Dr. Gans has been practicing medicine since 1994, and has focused on pediatric infectious diseases since 1998 at Stanford University Medical Center. Ex. A, filed May 23, 2017 (ECF No. 49-1) ("Gans CV"). She is currently an associate professor in the Department of Pediatrics and Division of Pediatric Infectious Disease at Stanford University. Gans CV at 1. Dr. Gans is board certified in both pediatrics and pediatric infectious diseases. *Id.* The majority of her time is spent in a clinical setting caring for children with infections, including immunocompromised children. Gans First Rep. at 1. Dr. Gans also does research in the field of infectious disease and immune responses, including responses to measles, mumps, and varicella vaccines in several populations such as normal hosts, HIV-infected children, premature children, and children who have received organ transports. *Id.* She serves on several regulatory boards overseeing the safety of vaccines, NIH study groups, and is a member of the Pediatric Infectious Disease Society Committee on Vaccines. *Id.*

First Report

Like Dr. Byers, Dr. Gans's first report includes a summary of E.R.'s medical records and history. Gans First Rep. at 1. Although E.R. was seen on multiple occasions for infections, she had no history of adverse events following vaccination—including the February 2012 vaccinations. *Id.* E.R.'s immunology records also revealed "normal function except for a decreased NK and CTL function." *Id*. at 2. Thus, Dr. Gans agreed with Dr. Byers that E.R. possessed an immunodeficiency (functional NK cell deficiency ("FNKD")) that predated and/or was unrelated to the vaccinations in question (although as discussed below she did not concede this immunodeficiency made an adverse vaccine reaction more likely). *Id.* at 10-11.

Dr. Gans directly disputed Dr. Byers's contention that E.R. had experienced a varicella reactivation manifesting as orolabial blisters. In support, she cited a number of different

evidentiary points. First, she emphasized treater views. E.R.'s immunologist, rheumatologist, and infectious disease specialist all concluded that E.R.'s facial lesions were the result of her underlying immunodeficiency and consistent with HSV—not manifestations of a varicella reactivation. Gans First Rep. at 2-4. No treaters had ever proposed anything comparable to Dr. Byers's contention.

Second, Dr. Gans observed that the clinical presentations of HSV and VZV are distinguishable—and E.R.'s presentation was more consistent with an HSV infection/reinfection. Gans First Rep. at 6. Although HSV and VZV are both herpes viruses with the capacity for latency, HSV reactivation is more frequent compared to VZV, which is rarely repetitive—whether in immunocompromised hosts or vaccinated individuals. *Id.* at 8. In addition, orolabial lesions are the most common manifestation of HSV, reflecting the initial infection site, its latency in the dorsal root ganglion of the TG nerve, and reactivation along the nerve's mandibular branch (hence around the mouth). *Id.*; S. Spruance et al., *The Natural History of Recurrent Herpes Simplex Labialis; Implications for Antiviral Therapy*, 297 (2)69 N. Engl. J. Med. 1-7 (1977), filed as Ex. A, Tab 4 on June 13, 2017 (ECF. No. 50-4) ("Spruance"). Such lesions can occur *without* a known or prior-identified primary infection of HSV. Gans First Rep. at 8. In Spruance, daily examinations were performed on 80 patients with recurrent herpes simplex labialis. *Id.* at 1. Frequent lesions occurred most often on the outer third of the upper or lower lip. *Id.* at 2. And nine of the total patients considered (24%) did not have virus recovered from any of the swab specimens. *Id.* at 2-3.

Also bearing on HSV reactivation is whether the patient in question is immune-compromised, like E.R. As Dr. Gans explained, individuals with NK cell deficiencies in particular have a specific vulnerability to recurrent HSV. Gans First Rep. at 11; C. Lopez et al., *Correlation Between Low Natural Killing of Fibroblasts Infected with Herpes Simplex Virus Type 1 and Susceptibility to Herpesvirus Infections*, 147 J. Infect. Dis. 1030-37 (1983), filed as Ex. A, Tab 7 on June 13, 2017 (ECF No. 50-7); E. de Vries et al., *Identification of an Unusual Fgc Receptor IIIa (CD16) on Natural Killer Cells in Patient with Recurrent Infections*, 88 Blood 3022-27 (1996), filed as Ex. A, Tab 8 on June 13, 2017 (ECF No. 50-8); B. Ornstein et al., *Natural Killer Cell Functional Defects in Pediatric Patients with Severe and Recurrent Herpesvirus Infections*, 207 (3) J. Infect. Dis. 458-68 (Feb. 2013), filed as Ex. A, Tab 9 on June 13, 2017 (ECF No. 50-9) ("Ornstein"). Ornstein's authors hypothesized that possession of an NK cell-oriented immunodeficiency "may predispose patients to herpesvirus infections." Ornstein at 459. To test this, Ornstein conducted a case-control study of 18 patients with a history of recurrent or severe HSV infections (78 percent of whom displayed recurrent orolabial or orofacial lesions), comparing them to 20 healthy controls. *Id.* Five of the 18, or 28%, possessed "potentially relevant NK cell functional and phenotypic abnormalities," suggesting to the article's authors that there was a likely association. Gans First Rep. at 9; Ornstein at 467. Thus, E.R.'s immunodeficiency was "sufficient to be the sole cause of her constellation of symptoms." Gans First Rep. at 7.

VZV reactivation is inherently different, in Dr. Gans's estimation, and is less common. Even in immunocompromised children (like E.R), reactivation [after vaccination] is "very diminished compared with natural disease." Gans First Rep. at 8. One study found only 13 out of 548 children with acute lymphocytic leukemia who received the live attenuated vaccine strain for varicella later developed VZV. *Id.*; I. Hardy et al., *The Incidence of Zoster After Immunization with Live Attenuated Varicella Vaccine. A Study in Children with Leukemia*, 325 (22) N. Engl. J. Med. 1545 (1991), filed as Ex. A, Tab 15 on June 13, 2017 (ECF No. 51-5) ("Hardy"). In Hardy, a subgroup of vaccinated children were matched to a control group of children who had natural varicella infection either before or after the diagnosis of leukemia. Hardy at 1545. Analysis of the Hardy subgroup found the incidence of VZV to be lower in the immunized group compared to those who had experienced a natural infection. *Id*. And reactivation of VZV has not been reported in vaccinated immunocompromised individuals who did not have an initial varicella rash. *Id.* at 1547; Gans First Rep. at 8. E.R. had herself not displayed any initial varicella rash. Gans First Rep. at 9.

The location of clinical manifestations of VZV reactivation is similarly distinguishable from HSV reactivation. Because vaccines are administered peripherally, i.e. in an arm, reactivation of a vaccine VZV strain so administered (whether to an immunocompetent and immunocompromised host) is more likely to occur in the trunk or extremities. Gans First Rep. at 8. When manifesting on the face, VZV reactivation associated with the varicella vaccine most commonly is evident clinically along the *ocular* branch of the TG nerve—not orolabially as here. *Id.* at 8; D. Guffey et al., *Herpes Zoster Following Varicella Vaccination in Children*, 99 (3) Cutis 207-11 (Mar. 2017) filed as Ex. A, Tab 17 on June 13, 2017 (ECF No. 51-7), at 208 ("Guffey"). Thus, out of 23 cases considered in Guffey, only five involved presentation on the face, with four confirmed instances of "Herpes Zoster Ophthalmicus," meaning around the eyes. Guffey at 209-10. And this kind of manifestation on the face is *itself* uncommon. Gans First Rep. at 8; Hardy at 1545 (only one out of thirteen vaccinated immunocompromised individuals developed VZV TG nerve reactivation, and only after exposure to wild type varicella). In addition, the majority of VZV reactivation cases occur years after vaccination, with the earliest recorded of which Dr. Gans was aware happening two months after vaccination. Gans First Rep. at 8.

E.R.'s "entire clinical picture," Dr. Gans concluded, was "most consistent with the diagnosis of Herpes Simplex Virus-1 infection with recurrent orolabial disease," not VZV. Gans First Rep. at 9. In so opining, Dr. Gans took issue with Dr. Byers's argument that E.R. likely did not have an HSV infection because testing had not confirmed it. Rather, laboratory tests of E.R.'s orolabial lesions were insufficient to isolate the HSV virus, and therefore, the fact that E.R. had not tested positive for the presence of antibodies confirming the HSV infection did not definitively rule it out. *Id.*

In support of such contentions, Dr. Gans reviewed what she deemed the diagnostic limitations of serologic testing intended to reveal the presence of an HSV infection in children. Timing of the testing, for example, could produce inconclusive results. Viral isolation is most effective when samples are taken within 24 hours of a lesion's appearance, for not long thereafter the viral recovery rate would drop sharply once the lesions began to crust over and heal. Gans First Rep. at 7; A. Singh et al*., The Laboratory Diagnosis of Herpes Simplex Virus Infections*, 16 (2) Can. J. Infect. Dis. Med. Microbiol. 92-98 (Mar.-Apr. 2005), filed as Ex. A, Tab 10 on June 13, 2017 (ECF No. 50-10). Here, however, the September 26, 2013 samples from E.R.'s lesions were taken while E.R. was taking acyclovir (which might suppress the infection by itself). Gans First Rep. at 4. Then, other samples were taken two weeks after E.R. stopped taking acyclovir—but from a scabbed lesion. *Id.*

Also reducing the utility of HSV testing was the fact that test sensitivity was lower in patients with recurrent HSV episodes. Gans First Rep. at 7.[7] And more generally, the presence of "antibodies to one microorganism does not predict seropositivity to other organisms," since the localized nature of the infection reduces the likelihood that it could be detected systemically, i.e. in the blood. *Id*. at 9. Serologic tests for HSV "'should be used with caution, if at all, in children under 14" and that "[n]o test for antibodies to HSV-1 or HSV-2 can be considered to be completely accurate in determining whether a person has or has not been infected with HSV." Ashley at 235. As a result, in Dr. Gans's experience clinicians relied far more on the clinical manifestations and response to antiviral therapy to diagnosis HSV rather than serologic tests. Gans First Rep. at 7.

While defending the possibility of an HSV infection/reinfection despite negative test results, Dr. Gans discounted Dr. Byers's argument that negative testing results for a varicella infection obtained in E.R.'s case were meaningless, simply because that testing could not be specific for the vaccine strain version. Gans First Rep. at 9. Dr Gans maintained in response that PCR testing could detect *both* wild type and vaccine strain of varicella, even though it could not differentiate between the two "since the homology of strains are too close and can only be differentiated by more detailed genetic analysis." *Id.* at 9-10. E.R.'s negative varicella virus culture was thus, in her view, still significant, since such a culture would have detected the presence of *some* form of active VZV infection, regardless of its source. *Id.* at 10.

Finally, Dr. Gans took issue with Dr. Byers's statement that the MMR vaccine was immunosuppressive (and thus could have contributed to E.R.'s alleged infectious process). Gans First Rep. at 10. Dr. Gans acknowledged the immunosuppressant nature of the measles disease when caused by a *wild virus* infection, but maintained there was no reliable medical or scientific support for the contention that the measles *vaccine* can have the same effect. *Id.* On the contrary,

[7] Although Dr. Gans referenced an item of literature in her report in support of this contention, it does not appear to have been filed. *See* ECF No. 51-1.

one study emphasized that the measles vaccine stimulates infants' immune system in an overall-*protective* manner, resulting in "a survival advantage for all-cause mortality, not just measles." *Id.*; A. Fisker et al., *Reduced All-Cause Child Mortality After General Measles Vaccination Campaign in Rural Guinea-Bissau*, 34(12) Pediatr. Infect. Dis. J. 1369-76 (Dec. 2015), filed as Ex. A, Tab 26 on May 23, 2017 (ECF No. 50-26). The MMR vaccine thus could not credibly be portrayed as an immunosuppressive agent that increased the likelihood of E.R. experiencing a VZV reactivation. Gans First Rep. at 10.

Second Report

Dr. Gans's second report largely discussed issues raised in Dr. Byers's second report. First, Dr. Gans addressed in additional detail Dr. Byers's argument that negative HSV test results evident in the medical record undercut the conclusion that E.R.'s blisters reflected an HSV infection. Gans Second Rep. at 1-2. She noted in reaction that Dr. Byers had provided only one paper in support of her claim that serologic methods and sensitivity has advanced since 2001, making it more likely testing would reveal the HSV infection were it present. Li et al., *Automated Chemiluminescent Immunoassay in Typing Detection of IgG Antibodies Against Herpes Simplex Virus*, 30 (5) J. Clinical Lab. Analysis 577-80 (2016), filed as Ex. 27 on April 11, 2018 (ECF. No. 60-1) ("Li").

But Dr. Gans deemed Li distinguishable. Li studied HSV testing of pregnant women with a mean age of 31—not children. Li at 577. Moreover, the assay/test in question "was not compared in performance to any other assay as thus no superiority can be established." Gans Second Rep. at 1; Li at 577-78. In contrasts, Ashley had used several serological tests in evaluating the effectiveness of HSV testing in children. Gans Second Rep. at 2; Ashley at 232-37. And Ashley had concluded that "'HSV type specific tests differ in their sensitivity and in their time to seroconversion and *should be interpreted with great caution* if used for paediatric sera." Ashley at 236 (emphasis added). Accordingly, serologic assays could not alone rule out HSV infection in children. Gans Second Rep. at 2. Indeed, they were unreliable evidence generally, since recurrent orolabial disease is a localized infection that does not necessarily produce a systemic infection or response that serologic testing would detect in the first place. *Id*. at 3.

Second, Dr. Gans attacked Dr. Byers's contention that E.R.'s HSV infection, which first presented in February 2012, could have begun after the initial evidence of facial "rash," since the record revealed some evidence of IgM (which would be by definition more recent) HSV antibodies as of January 2014. Gans Second Rep. at 2. Dr. Gans maintained that the indeterminate HSV IgM levels measured at this time would only have established a more recent, active infection "if a) the test was repeatedly positive and not indeterminate or if b) repeat testing in 2-4 weeks showed a rise in IgG." *Id.* But neither was later reported in E.R.'s case. *Id.* Thus, evidence of the presence of IgM in January 2014 was in Dr. Gans's opinion a nonspecific finding that subsequent testing never corroborated as significant. *Id.*

Dr. Gans further questioned Dr. Byers's argument about the significance of a positive VZV finding for E.R. based on testing performed in May 2013. Dr. Gans pointed out that as of this date, "E.R. was vaccinated and *would be expected to be positive*, therefore this does not link the vaccine to the oral lesions." Gans Second Rep. at 2 (emphasis added). She also reiterated the fact that no VZV virus was isolated from E.R.'s lesions after culturing. *Id.* at 1. And she challenged Dr. Byers's proposition that LabCorp (a prominent lab testing company) only reports findings specific to the wild type varicella virus, noting that this assertion lacked substantiation. *Id.* at 2.

Dr. Gans added that she did not question the scientific possibility of post-vaccination varicella reactivation, but rather disputed that such a reactivation would manifest orolabially, as occurred here. Gans Second Rep. at 3. HSV orolabial lesions are common because HSV reactivates along the mandibular branch of the TG nerve, while VZV reactivation is almost exclusively seen on the face along the *ocular* branch of the TG nerve. *Id.*; Hardy at 1545. Thus, "the mode of viral acquisition and the pattern of reactivation based on pathophysiology of the virus" support the conclusion that E.R.'s rash was the product of an HSV infection/reactivation, not varicella reactivation. *Id.*

Third Report

Dr. Gans's third report mostly responded to questions posed by the previous special master handling this case. One such question pertained to varicella reactivation generally. As Dr. Gans explained, varicella reactivation in any form (whether after wild infection or vaccination) could occur after the virus established latency in the dorsal root ganglia of a nerve, but no sooner than approximately 14-21 days from exposure. Gans Third Rep. at 1. The timing of reactivation would be somewhat dependent on varicella-specific T cell immunity, since this kind of "cellular" immune response to viral replication could enable or hinder reactivation depending on how robust it was. *Id.*; J. Gnann & R. Whitley, *Clinical Practice. Herpes Zoster*, 347 (5) N. Engl. J. Med. 340-46 (Aug. 1, 2002), filed as Ex. D, Tab 1 on Feb. 24, 2020 (ECF. No. 86-2) ("Gnann"); V. Traina-Dorge et al., *Reactivation of Simian Varicella Virus in Rhesus Macaques after CD4 T Cell Depletion*, 93(3) J. Virol. (Feb. 1, 2019), filed as Ex. D, Tab 2 on Feb. 24, 2020 (ECF No. 86-3). And because of E.R.'s known underlying immune deficiency, Dr. Gans opined that she was predisposed to reactivation of *any* herpes virus - varicella and HSV equally. *Id.*

The timeframe of E.R.'s purported varicella vaccination was also addressed. As Dr. Gans had explained in prior reports, immune-compromised but vaccinated children (like E.R.) were likely to experience post-vaccination varicella reactivation far sooner than immune-competent vaccinated children. Gans Third Rep. at 1; Hardy at 1545-50. But even that relatively shorter timeframe was not particularly fast. The shortest time to reactivation for the immune-compromised group was 2.5 months, with an average time to reactivation of 3.3 years. Gans Third Rep. at 1; Guffey at 208. Because E.R.'s history revealed purported reactivation *within two days* of

vaccination, persisting for a year or more later, Dr. Gans concluded that "[t]here is no biological plausibility" that E.R.'s varicella vaccination on February 20, 2012 could have caused those lesions. Gans Third Rep. at 1.

Another question posed by the special master was the significance of the acyclovir treatments E.R. had been receiving in the relevant time period. Gans Third Rep. at 2. As Dr. Gans explained, acyclovir is effective in treating both HSV and VZV. *Id*; J. Gnann et al., *Acyclovir: Mechanism of Action, Pharmacokinetics, Safety and Clinical Applications*, 3(5) Pharmacotherapy 275-83 (Sep.-Oct. 1983), filed as Ex. D, Tab 5 on Feb. 24, 2020 (ECF No. 86-6), at 275. However, varicella is "2-8 times less susceptible to acyclovir and requires much higher doses to control than HSV." Gans Third Rep. at 2; K. Biron & G. Elion, *In Vitro Susceptibility of Varicella-Zoster Virus to Acyclovir*, 18 (3) Anitmicrob. Agents Chemother 443-47 (Sep. 1983), filed as Ex. D, Tab 6 on Feb. 24, 2020 (ECF No. 86-7).

Review of the pharmacologic prescription guidelines for treatment of HSV or reactivated VSV in immunocompromised children confirmed to Dr. Gans that the medicinal course E.R. had received was consistent with treatment aimed at addressing an HSV infection. HSV was more likely to present in a recurring form, consistent with what E.R. experienced, and therefore treaters would understand that it would require a mix of higher general vs. lower suppressive doses, depending on the level of disease activity (and associated need to control lesion outbreaks). Gans Third Rep. at 3. A treatment note from E.R.'s medical record was cited by Dr. Gans as confirming that in this case, acyclovir had been prescribed at dosage levels intended for HSV rather than a VZV reactivated infection. *Id.*; Ex. 1 at 5.

III. Procedural History

This case was initiated in February 2015. ECF No. 1. The parties attempted to engage in settlement negotiations in the months following the claim's filing but were unsuccessful. Petitioners thereafter filed an expert report on January 20, 2017. Report, dated Jan. 20, 2017 (ECF No. 41). Respondent's Rule 4(c) Report and expert report were filed on March 23, 2017, and through these filings Respondent maintained this case was inappropriate for compensation under the Act. Rule 4(c) Report, dated Mar. 23, 2017 (ECF No. 48). Respondent filed a supplemental expert report on May 24, 2018. ECF No. 62. In 2020, the special master to whom the matter was originally assigned set a schedule for briefing ruling on the record. The parties filed their briefs, and then the matter was reassigned to me in January 2021. The case is ripe for resolution.

IV. Parties' Respective Arguments

Petitioners maintain that E.R. suffered, and continues to suffer, recurrent varicella/herpes zoster infections as a result of an adverse reaction to the vaccine virus contained in the Proquad vaccine (which contains both MMR and live-virus varicella-zoster virus) she was administered on February 20, 2012. Mot. at 1. This is the lynchpin of their argument; they do not contend, in the alternative, that E.R. could have had an HSV infection that these vaccines stimulated or enabled, and the entirety of their causal showing revolves around arguments about varicella latency and reactivation. Rather, Petitioners maintain that there is no evidence E.R. had an HSV infection before vaccination, and that she never tested positive for HSV antibodies. *Id.* at 11-12.

The vaccine Oka strain of the VZV, Petitioners argue, never leaves the body but becomes latent in the dorsal root ganglion. Mot. at 10. In E.R.'s case, the VZV continues to reactivate—because of her existing immunodeficiency that prevents her body from containing the virus—travelling from the dorsal root ganglia down the nerve to the skin where it forms a lesion. *Id.* In addition, VZV is known to establish latency in the dorsal root ganglion of the TG nerve, and E.R.'s lesions occurred along the mandibular branch of that nerve. *Id.* at 12.

Petitioners deem E.R.'s initial presentation of symptoms within 48 hours of vaccination as medically reasonable, expanding somewhat on a point not fleshed out in Dr. Byers's reports. Mot. at 10-11. They argue that medical literature establishes varicella infection can occur within a day of vaccination. *Id.* at 12; S. Galea et al., *The Safety Profile of Varicella Vaccine: a 10-Year Review,* J. Infect. Disease 197, S165-69 (2008), filed as Ex. 38 (ECF No. 85-1) ("Galea"). Galea observed from adverse event passive surveillance reporting approximately 3,200 instances of rashes up to 42 days after vaccination (out of over 16,600 total cases of adverse events), with wild-type VZV rashes occurring within 1-20 days, while the period for vaccinated individuals was longer (5-42 days). Galea at S166. Even though Galea facially suggests onset would be shorter for rashes attributable to the wild virus, Petitioners maintained the distinction was irrelevant, especially since it had not been established E.R. was ever exposed to wild varicella. Mot. at 14.

Respondent disputes Petitioners' entitlement to damages, arguing that preponderant evidence supports the conclusion that she suffered from a recurrent HSV infection. Opp. at 8. Respondent notes E.R.'s immunodeficiency predisposed her to recurrent HSV infections. *Id.* Additionally the evidence does not support onset of VZV reactivation occurring in a 48-hour timeframe. *Id.* at 12-13. In so arguing, Respondent underscored the fact that Galea distinguished between onset for wild virus-caused varicella infection and vaccine strain-caused, and that its authors actually determined that *most* cases involving onset within two weeks of vaccination were due to a wild virus infection. *Id.* at 13.

Further, Respondent maintained that Petitioners failed to show that E.R.'s alleged injury was vaccine caused. Opp. at 1. Respondent distinguished E.R.'s clinical presentation, which is consistent with HSV, from the expected clinical presentations of varicella infection. *Id.* at 8. Respondent also argues that there is significant clinical evidence that was sufficient for multiple treating doctors to diagnose E.R. with HSV, despite the lack of confirmatory serologic testing. Id. at 11. As a result, the Petitioners cannot preponderantly establish that the varicella vaccine was the cause of E.R.'s injury. *Id.*

Petitioners' Reply reiterates her claim primarily focuses on the contention that E.R. "suffered from vaccine caused varicella zoster infection," *not* an HSV infection. Reply at 1. Indeed, they highlight that she had received a second dose of the vaccine "containing the very virus that was causing her injury," making it the more logical explanation for the subsequent blistering. *Id.* They again note that the HSV infection proposed by Respondent is not backed up by test results, and propose that the immune deficiency she possessed could explain why she had difficulty responding to the stress of the vaccination, and maintain the varicella infection is consistent with a facial outbreak. *Id.* at 1-2. They admitted, however, that it cannot be determined whether E.R.'s recurrent varicella infection reflects reactivation of the vaccine strain she first received in 2009, or a "super infection" attributable to the second dose—although the result is the same. *Id.* at 2. Petitioners also attempted to defend their reading of Galea regarding onset, arguing that because the studied population had never experienced a prior wild virus infection, and the specific sources of their infection were not corroborated by PCR testing, Respondent was incorrect in maintaining that *any* 1-14 day onset was likely due not to vaccination. *Id.* at 3-4.

V. Applicable Law

A. *Standards for Vaccine Claims*

To receive compensation in the Vaccine Program, a petitioner must prove that: (1) they suffered an injury falling within the Vaccine Injury Table (i.e., a "Table Injury"); or (2) they suffered an injury actually caused by a vaccine (i.e., a "Non-Table Injury.) *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano*, 440 F.3d at 1320. In this case, Petitioners do not assert a Table claim.

For both Table and Non–Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct.

476, 486 (1984) (explaining that mere conjecture or speculation is insufficient under a preponderance standard). On one hand, proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). But on the other hand, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non–Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health and Hum. Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury." Each *Althen* prong requires a different showing and is discussed in turn along with the parties' arguments and my findings.

Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

However, the Federal Circuit has *repeatedly* stated that the first prong requires a preponderant evidentiary showing. *See Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1360 (Fed. Cir. 2019) ("[w]e have consistently rejected theories that the vaccine only "likely caused" the injury and reiterated that a "plausible" or "possible" causal theory does not satisfy the standard"); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010). This is consistent with the petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted). If a claimant must *overall* meet the preponderance standard, it is logical that they be required also to meet each individual prong with the same degree of evidentiary showing (even if the *type* of evidence offered for each is different).

Petitioners may offer a variety of individual items of evidence in support of the first *Althen* prong, and are not obligated to resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health &*

Human Servs., 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). No one "type" of evidence is required. Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu,* 569 F.3d at 1380. However, even though "scientific certainty" is not required to prevail, the individual items of proof offered for the "can cause" prong must *each* reflect or arise from "reputable" or "sound and reliable" medical science. *Boatmon,* 941 F.3d at 1359-60.

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356–57 (2011), *aff'd without opinion*, 475 F. App'x. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the

phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11–355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains

reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are automatically deemed accurate, or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous

medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

However, in the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings—e.g., the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743

(quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioners' case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015–5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Disposition of Case Without Hearing*

I am resolving this claim on the papers, rather than by holding a hearing, consistent with the determination of the prior special master to whom the case was assigned, and the parties have not in their filings opposed this mechanism for resolution. *See* Joint Status Report, dated February 11, 2021 (ECF No. 98) ("2021 Joint Status Report"). The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Human Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Human Servs.,* No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Human Servs*., 38 Fed. Cl. 397, 402–03 (1997) (determining that special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417; *Murphy v. Sec'y of*

Health & Human Servs., No. 90-882V, 1991 WL 71500, at *2 (Ct. Cl. Spec. Mstr. Apr. 19, 1991).

ANALYSIS

I. Varicella Reactivation and Relevant Vaccine Act Cases[8]

Because the capacity of the varicella virus to become latent in the body, then reactivate later, is squarely placed into issue by Petitioners' causation theory, some brief discussion of what is scientifically and medically known about the mechanisms involved in this process, and how such a reactivation typically manifests, is warranted.

An initial VZV infection (which is often termed "chickenpox") is caused by varicella—a highly contagious virus that impacts almost every person before adulthood. *See Atlas of Pediatric Physical Diagnosis* 444 (5th ed. 2007).[9] Its symptoms, usually occurring after a 10–21 day incubation period, include fever, malaise and the itchy rash for which it is best known. *Id.* A VZV infection is usually self-limiting and mild, although severe and potentially-fatal complications may arise, such as secondary bacterial infections or neurologic impacts (encephalitis). *Id.* Indeed, varicella is especially dangerous to children and the immune-compromised.

A varicella infection is usually diagnosed from clinical indicia, such as the presence of the rash commonly associated with it. Gans First Rep. at 7. However, some laboratory testing can also confirm its presence. Evaluation of the virus's presence from direct testing of skin lesions/vesicles is most common, although strain identification can also assist in distinguishing the wild virus from vaccine-associated strains. Byers Third Rep. at 2. It is treated with the antiviral drug acyclovir. *See generally* Mayo Clinic, *Acyclovir (Oral Route, Intravenous Route) Description and Brand Names*, available at https://www.mayoclinic.org/drugs-supplements/acyclovir-oral-route-intravenous-route/precautions/drg-20068393?p=1 (last visited Aug. 12, 2021).

One feature of VZV distinguishing it from other viral infections is its capacity for latency and subsequent reactivation. *Pearson v. Sec'y of Health & Human Servs.,* No. 16-9V, 2019 WL

[8] Decisions from different cases do not *control* the outcome herein, with only Federal Circuit decisions setting legal standards to which new claims must adhere. *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 1351, 1358-59 (Fed. Cir. 2019); *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). Nevertheless, special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Human Servs.,* 76 Fed. Cl. 328, 338-39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would thus be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions.

[9] This item of literature is a treatise, and it is cited for definitional purposes only.

3852633, at *15 (Fed. Cl. Spec. Mstr. 2019) ("varicella zoster reactivation is a relatively common ailment—approximately 1 million new cases are diagnosed annually in the United States, and 90% of these patients are immunocompetent"). After exposure to the virus in childhood, the immune system of most individuals is successful in eliminating it, but (for reasons not totally understood by medical science) it often remains dormant/latent in the central nervous system, "hiding" within the sensory ganglia. Uebe at 442. Thereafter, the virus can reactivate in adulthood, causing a varicella zoster infection, or "shingles," which is characterized by a painful rash localized to the part of the body where the infection was latent, and usually following along the dermatome.[10] W. Van Heerden, *Oral Manifestations of Viral Infections*, 48(8) SA Fam. Pract. 20-24 (2006), filed as Ex. 31 on Apr. 11, 2018 (ECF No. 60-5), at 22. Although shingles usually resolves in a few weeks, it can have associated secondary symptoms, or lead in some cases to ongoing nerve pain or neuralgia. *Pearson,* 2019 WL 3852633, at *15. Only those previously infected with VZV can experience shingles, and it most commonly afflicts individuals over 50 years old (and thus the virus's latency can be years long).

Importantly, the clinical manifestations of shingles/varicella reactivation are distinguishable from an initial varicella/chickenpox infection. Gans First Rep. at 6. Shingles is more common in those whose immune systems are compromised (whether due to aging, receipt of medical treatments known to be immunosuppressive, or psychologic stress). *Shingles*, Mayo Clinic (June 10, 2020, 5:17pm), https://www.mayoclinic.org/diseases-conditions/shingles/symptoms-causes/syc-20353054.

As noted above, Petitioners maintain either that (1) E.R.'s inability to immunologically contain the varicella virus resulted in recurrent varicella infections, triggered by the second dose, and/or (2) the varicella virus simply reactivated in E.R. (again due to vaccine triggering) from the dorsal root ganglia—in either case leading to the maxillary branch of the trigeminal nerve resulting in lesions on the chin and lips. Petitioners have in prior Vaccine Act causation cases[11] successfully demonstrated that the varicella vaccine directly caused a *subsequent varicella infection*. *See, e.g.*, *Hayes v. Sec'y of Health & Human Servs*., No. 18-804V, 2019 WL 3821992 (Fed. Cl. May 14, 2019) (reactivation conceded by Respondent)*; Haigler v. Sec'y of Health & Human Servs.,* No. 11-508V, 2013 WL 5428103 (Fed. Cl. Spec. Mstr. Sept. 5, 2013) (varicella vaccine caused encephalopathy due to reactivation); *Casey v. Sec'y of Health & Human Servs*., No. 97-612V, 2005 WL 3597263 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) (varicella vaccine caused encephalo-

[10] The dermatome is the area of skin supplied with afferent nerve fibers by a single spinal nerve. *Dorland's* at 491. Each segment is named for the principal spinal nerve serving it—the trigeminal, cervical, thoracic, lumbar, or sacral segments. *Id.*

[11] There is also a Table claim for injuries associated with varicella reactivation. *See* 42 C.F.R. § 100.3(a)(X)(C). But no such claim is asserted herein, and none would be tenable.

myelo-radiculo-neuropathy attributable to reactivated infection). Accordingly, the general concept of varicella reactivation attributable to the same vaccine constitutes a reliable basis for a Vaccine Act claim.

There are, however, some important limitations on the theory that bear on this case. In particular, onset from vaccination to injury in such cases was a matter of a few weeks—not days, as alleged here. *See,* e.g., *Hayes*, 2019 WL 3821992 (onset of infection two to three weeks post-vaccination);[12] *Haigler*, 2013 WL 5428103, at *17–18 (onset of encephalopathy within two weeks of receipt of varicella vaccine); *Casey*, 2005 WL 3597263, at *1–2 (onset of neurologic injuries began four to six weeks post-vaccination). I otherwise have found no causation-in-fact decisions in which a petitioner established non-varicella injury—an injury associated with a *distinguishable* viral infection—due to a reactivated varicella infection or triggered by a second dose of varicella vaccine.

II. Petitioners Have Not Established that E.R. Experienced Varicella Infection or Reactivation

As in many Vaccine Program cases, identifying whether the alleged injury actually occurred is critical to this claim's resolution. *Broekelschen*, 618 F.3d at 1346. Petitioners expressly argue that E.R. experienced a *varicella* infection—not HSV. Mot. at 1, 10. Although it cannot be established with certainty that E.R. had a documented HSV infection prior to the February 20, 2012 vaccination, the record still preponderates in favor of the conclusion that E.R.'s clinical presentation was *most consistent* with HSV, not with varicella. And the record does not support the determination that E.R. was experiencing a varicella infection or reactivation.

Contrary to Petitioners' assertion that "zero" medical record evidence supports this conclusion ("Mot. at 11), there is in fact ample evidentiary support for it. As explained by Respondent's experts, HSV reinfection is common, occurring in 20-40% of infected individuals—and can even occur *without* a prior known primary infection. Gans First Rep. at 7; Spruance at 70. It also frequently occurs in the orolabial area, as happened here. Gans First Rep. at 7. In addition, immunocompromised patients such as E.R. are at a higher risk of recurrence—with NK cell deficiency being associated with recurrent HSV. *Id.*; *see generally* Ornstein.

The record further illustrates that several of E.R.'s treaters—Drs. Fulkerson, Lopez-Marti, and Henrickson—all concluded, based on their direct treatment of E.R., that her presentation was consistent with an HSV infection. *See, e.g.*, Ex. 1 at 36-41, 204-5; Ex. 2 at 152-53, 264-65. Although treater views are never sacrosanct in Program cases, they are deserving of weight. And

[12] The ruling on entitlement in *Hayes* does not set forth such facts, which are instead found in Respondent's Rule 4(c) Report conceding entitlement. *See Hayes* Rule 4(c) Report, dated May 9, 2019 (ECF No. 24).

Dr. Gans persuasively explained in her third report that the acyclovir treatment E.R. received (a medication not reserved exclusively for varicella, as Dr. Byers admitted (Byers Third Rep. at 2)) was calibrated toward the treatment of a recurrent HSV infection. Gans Third Rep. at 2-3.

Petitioners' efforts to rebut this evidence and its implications were largely limited to their contention that it was inconceivable a child could have an HSV infection in the absence of confirmatory serologic testing. Mot. at 11. It is true that this kind of confirmatory test result evidence is lacking in the medical record. But its absence *does not completely rebut treater conclusions*. This is because this data point is not by itself dispositive, but must instead be weighed against all the other record evidence that is consistent with an HSV infection. Performing that weighing, as I am called upon to do, leads to the conclusion that preponderant evidence best supports the conclusion that E.R.'s lesions were the product of HSV, not varicella – even if the HSV infection was never corroborated as a certainty.

Moreover, the argument that the lack of serologic confirming test results is fatal to this determination overstates the reliability of such testing generally. In particular, and as Dr. Gans persuasively explained, serologic testing for HSV viral infections would not have high utility for children. Gans First Rep. at 7. And direct lesion testing would need to occur close-in-time to lesion formation to have value. *Id.*[13] The argument that one of the labs utilized by Petitioners in this case (LabCorp) is "widely known to perform testing of the highest accuracy" (Second Byers Rep. at 5) does not negate Dr. Gans's points.

Petitioners otherwise did not establish that a diagnosis of HSV infection based largely on clinical presentation would be *invalid* from a medical standpoint absent confirming lab results. To a degree, Petitioners seem to be demanding a level of certainty from Respondent on this point that the Program does not require of petitioners. Indeed, it is recognized in the Program that a claimant's post-vaccination injury might be determined to be idiopathic, meaning without identified explanation—and such conclusions often overcome a claimant's arguments that the Respondent has not "proven" an alternative cause, such as a different wild infection. *Egan v. Sec'y of Health & Hum. Servs.*, No. 05-1032V, 2009 WL 1440240, at *20 (Fed. Cl. Spec. Mstr. May 1, 2009) (noting that "in a high percentage of cases" no cause of a given injury can be identified). It therefore could well be the case that an HSV-like presentation is reasonably understood to reflect an underlying HSV infection, even where that infection could not be serologically confirmed.

[13] At the same time, Dr. Byers did not have much to say about why the blisters/lesions *themselves* did not test positive for VZV, and how that absence of confirmation did not otherwise harm her claims. *See* First Byers Rep. at 2, 3. The fact that E.R. tested positive for varicella antibodies in 2013 does not undercut this point, since, as Dr. Gans observed, E.R. had received two doses of the varicella vaccine – and therefore *should* have shown seropositivity in the wake of vaccination. Gans Second Rep. at 2.

I also note that the record does not support the alternative conclusion—that E.R.'s orolabial blisters and lesions were varicella—and Petitioners' arguments to the contrary were strained and unpersuasive. In particular, Petitioners failed to establish that varicella reactivation is consistent with E.R.'s actual presentation. Gans First Rep. at 4-5. E.R. was never diagnosed with or exhibited symptoms of shingles—the reactivated version varicella zoster infection commonly seen in adults. And reactivation of varicella zoster infection is in fact *far less likely* after vaccination, in comparison to exposure to the wild virus. Gans First Rep. at 8. In addition, the location of E.R.'s blisters/lesions was *not* consistent with shingles (HSV reactivation) when presenting on the face. Gans First Rep. at 2-4. Rather, shingles presentation is a unilateral vesicular eruption in a restricted dermatomal distribution, and when on the face is more likely around the eyes. *Id.* at 7; Gnann at 342; Gans Second Rep. at 5. Dr. Gans persuasively established that this phenotypic presentation is common to HSV, but not to varicella, and cited evidence in support. *See generally* Spruance, Guffey. A varicella reinfection after latency would far more likely occur in the periphery, closer to the situs of vaccination.

At bottom, the HSV infection as an explanation for E.R.'s clinical presentation was repeatedly embraced by knowledgeable treaters, even in the face of negative blood testing. This evidence was enough for her treaters, and they fashioned their medicinal treatment accordingly. Moreover, E.R.'s undisputed immune deficiency provided a compelling alternative explanation for why she would struggle with the HSV blisters—and Petitioners did not adequately rebut that possibility in their prima facie showing. *See Garner v. Sec'y of Health & Hum. Servs.*, 133 Fed. Cl. 140, 145-46 (2017).

As already noted, Petitioners' case relies heavily (if not wholly) on a determination that E.R.'s injury was a varicella infection attributable to reactivation. Because I have determined that this central contention lacks preponderant support, I need not conduct any *Althen* evaluation in this case (and will not therefore speculate on how Petitioners would have done had my determination been otherwise). *Monzon v. Sec'y of Health & Hum. Servs.*, No. 17-1055V, 2021 WL 2711289 at *21 (Fed. Cl. Spec. Mstr. June 2, 2021).[14]

[14] I do note, however, that even had I found that E.R. had experienced a varicella reactivation, Petitioners' claim would still have failed to satisfy all three *Althen* prongs – mainly because they have not preponderantly established that onset occurred in a medically reasonable timeframe (*Althen* prong three). The very item of literature Petitioners offer to support this aspect of their case, Galea, supports a *longer* timeframe for reactivation onset after receipt of varicella vaccine (no less than five days post-vaccination) than what E.R. experienced (lesions appearing one to two days post-vaccination). Galea at S166. Petitioners' argument that wild virus reinfections could not be distinguished herein from a vaccine-strain reinfection were unpersuasive – a dodge that ignored Galea's plain determination. *Id.* I also take some note of the fact that prior decisions in which reactivation of varicella has resulted in compensation all involved longer timeframes. *See,* e.g., *Hayes*, 2019 WL 3821992 (onset of infection two to three weeks post-vaccination); *Haigler*, 2013 WL 5428103, at *17–18 (onset of encephalopathy within two weeks of receipt of varicella vaccine). A one to two-day reactivation simply has not been preponderantly defended to be medically acceptable.

III. This Case was Properly Resolved Without a Trial

In ruling on the record, I am (consistent with the determination of the special master to whom this case was previously assigned) opting against holding a hearing. Determining how best to resolve a case is a matter that lies generally within my discretion, but I shall explain my reasoning (despite the fact that the parties acquiesced to the case's resolution in this manner).

Prior decisions have recognized that a special master's discretion in deciding whether to conduct an evidentiary hearing "is tempered by Vaccine Rule 3(b)," or the duty to "afford[] each party a full and fair opportunity to present its case." *Hovey*, 38 Fed. Cl. at 400–01 (citing Rule 3(b)). But that rule also includes the obligation of creation of a record "sufficient to allow review of the special master's decision." *Id*. Thus, the fact that a claim is legitimately disputed, such that the special master must exercise his intellectual faculties in order to decide a matter, is not itself grounds for a trial (for if it were, trials would be required in every disputed case). Special masters are expressly empowered to resolve fact disputes without a hearing—although they should only so act if a party has been given the proper "full and fair" chance to prove their claim.

No hearing was required to resolve the present claim in a fair manner. My decision to dismiss this case turned primarily on Petitioners' inability to show that E.R. suffered from a varicella reactivation. That determination could be made simply by careful review of the record plus the expert reports—and no hearing would have made a different result likely. In particular, there was no need for live testimony from the experts. Dr. Byers's expertise does not lie in diagnostic matters of the kind put into contention in this case. Petitioners otherwise have had ample opportunity to substantiate the claim. The special master to whom this case had originally been assigned first ordered the parties to brief a ruling on the record in *February 2020*, with both sides agreeing a year later that the matter was fully ripe for resolution. 2021 Joint Status Report at 1. Petitioners were not deprived of the chance to develop the record or make their best case.

CONCLUSION

For the aforementioned reasons, this claim is dismissed. In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this Decision.[15]

IT IS SO ORDERED.

s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[15] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.